RECURRENT TYPE I PNEUMONIA: SERUM TREATMENT OF TWO ATTACKS ONE MONTH APART:*

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As an illustration of several important points in the immunology and therapy of lobar pneumonia the following case is reported: Opportunity for complete investigation of the condition was not afforded, but enough data are on hand to make an interesting study.

Our knowledge of immunity—active or passive—in lobar pneumonia is still in a comparatively indefinite state.[1]

1. Does one attack confer any immunity?
2. Are successive attacks more liable to be caused by a pneumococcus of a different type or of the same type?
3. Does prophylactic inoculation with killed cultures produce immunity?
4. Can passive immunity be produced by the injection of antipneumococcus horse serum?

The blood of patients recovering from lobar pneumonia was shown[2] to possess, at the time of crisis and shortly after, the power to protect laboratory animals from lethal doses of the type of pneumococcus which caused the pneumonia. Specific antibodies, agglutinins[3] and opsonins[4] have been similarly demonstrated, but their demonstration, in some cases, becomes impossible within a relatively short time after recovery. Skin tests using bacterial antigens[5] have been tried but are as yet unsatisfactory. Complement-fixation tests[6] have not added to our information and no one has shown the presence of true pneumotoxin and antitoxin.[7] These statements show quite clearly that we obtain no practical aid from laboratory methods in demonstrating more than a fleeting immunity to lobar pneumonia following recovery.

Available information as to immunity afforded by an attack is extremely limited. That people have repeated attacks of pneumonia is well known, but the opportunity for studying several attacks in one individual is rarely offered, so that the degree of active immunity produced by one attack is still undetermined. A case in the Rockefeller series[8] is known to have suffered from sixteen attacks of pneumonia, the last two attacks being studied in the Hospital of the Rockefeller Institute. The bacteriologic history begins with the twelfth attack (1916), which is reported to have been caused by Pneumococcus Type I. The next attack (1916) was caused by Pneumococcus Type III and the fourteenth attack (1916) by Pneumococcus Type IV. During the fifteenth (1916) and sixteenth

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* From the Pneumonia Service, Boston City Hospital.

(1917) attacks Pneumococcus Type III was isolated. At the time of the last attack of pneumonia he also suffered from acute double otitis media, with cervical and submaxillary lymphadenitis. He was again admitted a year later (1918), suffering from chronic ethmoiditis, left; chronic sphenoiditis, left; acute otitis media, left; acute cervical adenitis, left. He received inoculations of heat-killed pneumococcus vaccine, including the three fixed types, in 1916, after his fifteenth attack and again at the time of his last admission. He has not had pneumonia since February, 1917.

This patient had five attacks of lobar pneumonia within a period of a little more than one year—three of these attacks were caused by the same organism, Pneumococcus Type III, which may have been harbored in an infected sinus. That he recovered from sixteen attacks of lobar pneumonia suggests some degree of immunity, but obviously not enough to prevent the attacks.

The only other patient observed in two attacks of pneumonia at that clinic[8] was a man who had a Pneumococcus Type I infection of the right lower lobe in March, 1918. He was treated with serum and recovered uneventfully. About one year later he returned with a typical right lower lobar pneumonia, again Pneumococcus Type I. He was desensitized, treated with serum and again recovered.

From February, 1919, when the pneumonia service was started at the Boston City Hospital, to May 1, 1920, there have been two cases other than the one reported in this paper, admitted twice with lobar pneumonia.

M. G., aged twenty-four years, admitted May, 1919; lobar pneumonia, Pneumococcus Type II; readmitted October, 1919; lobar pneumonia, Pneumococcus Type I.

F. P., aged seven years; admitted May, 1919; lobar pneumonia, Pneumococcus Type IV followed by pleural effusion; readmitted September, 1919, with lobar pneumonia, Pneumococcus Type II atypical.

No definite conclusions can be drawn from these four cases.

The efficacy of prophylactic inoculation, on the other hand, has been well demonstrated,[9] and from this fact we may infer that recovery from an attack leaves a certain immunity, the points in doubt being its degree and duration. An attack of typhoid fever usually produces complete and lasting immunity, whereas prophylactic inoculation must be repeated every few years. Arguing from analogy, an attack of lobar pneumonia should produce a much more satisfactory immunity than prophylactic inoculation, or, in other words, a very fair degree of immunity.

Blake and Cecil,[10] announcing the titles of their articles to appear in the coming numbers of the *Journal of Experimental Medicine*, speak of Paper V, "Active Immunity against Experimental Pneumococcus Pneumonia in Monkeys following Vaccination with Living Cultures of Pneumococcus," and Paper VI, "Active Immunity Following

Experimental Pneumococcus Pneumonia in Monkeys." They evidently have been able to demonstrate active immunity following an attack of lobar pneumonia in monkeys as well as after pro-prophylactic vaccination. This agrees with the current opinions on the subject of immunity in lobar pneumonia in man, and it is, as far as we know, the nearest approach to an actual demonstration that has been brought forth.

Lastly, that Type I, lobar pneumonia, may be aborted and cured by intravenous administration of Antipneumococcus Type I horse serum[11] is proof of the production of passive immunity. How long does this passive immunity last? For an absolute answer to this question the substance producing the immunity should be known and tested for until its disappearance from the blood stream. (The question of local immunity need not be discussed at this time.) Agglutinins, precipitins, opsonins and bacteriotropins are shown to disappear rapidly, but the exact duration of their presence in the serum has not been carefully worked out. Whether the curative effect of anti-pneumococcus serum depends on one or all of these factors,[12] or even others yet undescribed, is still a matter of conjecture; therefore the duration of passive immunity for pneumonia must at present remain undetermined. If we turn to a condition in which passive immunity has been carefully studied, *i. e.*, diphtheria, we see that this immunity diminishes very rapidly, so that it cannot be demonstrated at the end of four weeks.[13] There is no evidence that passive immunity to pneumonia lasts any longer than this. We fully realize the unreliability of this comparison, however, as a toxin-antitoxin mechanism in pneumonia has never been conclusively shown.

RECORD OF CASE.

J. B. Aged twenty-nine years; married; colored; meat handler.

Admitted. November 29, 1919.

Complaint. Cough, pain in chest.

Family History. Unimportant; wife and one child living and well; no miscarriages.

Personal History. Measles, mumps, whooping-cough and chicken-pox in childhood. Malaria nine years ago. Lobar pneumonia, left upper lobe (no bacteriology), April 19, 1918, in Boston City Hospital. Wassermann positive, April 30, 1918.

Nocturia. One to two times for past six months.

Venereal. Denied.

Habits. Coffee, two to three cups daily. Whisky, two to three drinks; beer, three or four drinks daily before prohibition. Tobacco, chews twenty cents worth a week.

Weight. Best 175 pounds, three months ago. Average, 165 pounds. Last weight, 166 pounds.

Present Illness. Sudden onset yesterday, November 28, 1919, with chill, pain in left side, severe malaise and bone aches. Cough with brown, sticky sputum. Last night vomited and developed "pleurisy pain" in the left chest.

Physical Examination. Well-developed and nourished colored man, complaining of severe pain on inspiration.

Lungs. Slight dulness below left clavicle. In this region and high in the left axilla breath sounds are bronchovesicular in quality, whispered and spoken voice sounds are increased and following cough there are persistent medium rales.

November 29. Wassermann strongly positive. Blood culture positive, Pneumococcus Type I. Sputum, mouse inoculation, Pneumococcus Type I. Skin test (horse serum), negative.

November 30. 11.30 A.M., 1 c.c. horse serum intramuscularly. 12.30 P.M., 100 c.c. antipneumococcus serum, Massachusetts State Board of Health Laboratory No. 50, given intravenously very slowly. 1.15 P.M., ten minutes after completion of serum treatment, patient developed a diffuse urticaria which was easily controlled by adrenalin, $\frac{1}{1000}$ solution ♏x followed in fifteen minutes by adrenalin $\frac{1}{1000}$ solution ♏vii.

December 1. Temperature normal; signs in chest slightly more marked than yesterday. White count, 20,200. Roentgen ray of chest: left diaphragm higher than right; left apex dense homogeneous shadow; pneumonia. Urine: albumin, slightest possible trace; sediment, few white blood cells.

December 2. Lungs clearing rapidly, temperature remains normal.

December 3. White count 5800.

December 4. Urine: albumin, 0; sediment, 0; Wassermann negative.

December 6. Lungs clear. Up and around ward. White count 7400.

December 8. Two nights ago patient complained of slight itching. There were a few urticarial wheals to be made out.

In other respects condition is absolutely normal. Patient insists on going home on account of illness of wife. To continue convalescence at home. Discharged cured.

Diagnosis: Lobar pneumonia, left upper lobe. Pneumococcus Type I.

From subsequent questioning it was learned that the patient remained quietly at home for several days, but felt so well and strong that about December 12 he returned to work in a meat market, which was damp and cold.

Second Admission. Admitted December 30, 1919 (thirty-one days after preceding admission).

Present Illness. Sudden chill while at work yesterday. December 29, slight headache and general malaise, cough with yellow sputum, which became reddish this morning. Vomited once.

Physical Examination. Over right upper lobe percussion note is dull; breath sounds are tubular; voice sounds tubular and nasal in quality. Few medium rales at left apex.

December 30. Sputum Pneumococcus Type I, Bacillus influenza. Blood culture, negative. Wassermann strongly positive.

December 31. White count 18,800.

12 M. Skin test (horse serum), very slightly positive (?). 1 P.M., 1 c.c. horse serum intramuscularly. 2 P.M., 100 c.c. Antipneumococcus Type I serum, Massachusetts State Board of Health Laboratory No. 51, administered intravenously, the first 30 c.c. given slowly over a period of thirty minutes and the remainder in fifteen minutes. No immediate reaction was noted during treatment, but twenty minutes later patient had a mild chill and complained of slight itching.

December 31. Roentgen-ray of chest; dense shadow localized in right axilla. Temperature fell during afternoon and night, reaching 99° rectal at 5 A.M. (January 1, 1920), but rose again to 103° rectal at 9 A.M.

January 1. 10 A.M. 100 c.c. Antipneumoccocus Type I serum (Laboratory No. 51) given intravenously; no immediate reaction; no chill.

January 2. Temperature, pulse and respiration fell gradually, reaching normal this morning. Patient looks and feels much better.

January 7. Lungs clear. Patient up one-half hour.

January 11. No signs of serum sickness, condition excellent.

January 11. Patient insists on going home. Has not had any evidence of serum sickness. Discharged cured.

Diagnosis: Lobar pneumonia in right upper lobe. Pneumococcus Type I and Bacillus influenza.

Patient has moved from former address since being discharged and has been lost track of. The question as to whether he ever had any serum sickness following his second pneumonia serum-treatment cannot be answered.

Discussion. Here, then, is a case of recurrent pneumonia Type I, the second attack occurring twenty-nine days after recovery from the first. The infecting organisms may quite possibly have remained in the patient's mouth during the period between the attacks.[14] He was, however, susceptible to a second attack within a month of the first one. To be remembered, in the consideration of this point, is the fact that the first attack was cut short on the third day of the disease by serum treatment. This unquestionably lessened the antigenic value of the first attack and minimized any active immunity which may be acquired in this manner. On the other hand the passive immunity obtained from the horse serum which enabled him to recover promptly from the first attack was not sufficient one month later to protect him from a second attack.

Another interesting phase of this case is the lack of sensitiveness to horse serum which the patient showed thirty-one days after receiving 100 c.c. of horse serum intravenously.

Longcope and Rackemann[15] in studying 25 cases treated with horse serum made the observations that in cases which escaped serum disease, precipitins and anaphylactic antibodies were not observed, whereas the skin reaction made its appearance irrespective of the amount of serum administered or the method of administration, and appeared whether or not serum disease developed. The skin hypersensitiveness became demonstrable much later, however, in patients who did not develop serum sickness than in those who did, and was first observed in one such case on the thirty-third day and in another on the fiftieth day. They concluded from their observations that serum disease depends on a reaction which takes place within the cells of the body and following which antibodies for horse serum are extruded into the circulation in great quantity. These antibodies dispense with the circulating antigen more or less rapidly.

We see, then, that if serum disease does not develop the circulating antigen may remain for a much longer period and the appearance of circulating antibodies be much delayed or reduced in amount.

Our case differs from their three cases, which escaped serum sickness, in that he did show six days after receiving the first dose of serum a few urticarial wheals. But in view of his subsequent freedom from sensitiveness we feel that it is not safe to place too great reliance on this observation, inasmuch as in the course of making routine ward notes another type of cutaneous lesion may have been mistaken for slight urticaria due to serum sickness. During the twelve days that the patient was under observation following his second course of treatment no sign of serum sickness was noted at any time. No subsequent history is obtainable. We explain his lack of sensitiveness, then, as due to his failure to react in the usual manner by having serum sickness. It is probable that sensitiveness would have developed in a longer period of time.

Conclusions. The development of any active immunity by an attack of lobar pneumonia Type I may be prevented in part or entirely by the early administration of antipneumococcus serum Type I.

Passive immunity obtained from antipneumococcus horse serum Type I may not protect against an attack of pneumococcus Type I pneumonia for more than one month.

Sensitiveness to horse serum is occasionally late in developing; therefore serum treatment of a patient who has recently received serum should not be omitted through fear of anaphylaxis without first testing the patient's degree of sensitiveness and attempting to desensitize him.

It is interesting to note the occurrence of two strongly positive Wassermann reactions, each while the patient's temperature was up, whereas one done during the afebrile period intervening was negative. In 1918 his Wassermann reaction was positive when he was afebrile.

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THE COLLOIDAL GOLD CURVE IN EPIDEMIC ENCEPHALITIS: A PRELIMINARY NOTE.*

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The occurrence of abnormal changes in the reaction of colloidal gold solution to the spinal fluid in epidemic encephalitis has not,

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* This paper is based upon cases which have been at Bellevue Hospital, New York, and has been written at the suggestion of Dr. Foster Kennedy, physician in charge of the neurological department. We wish to express our thanks to Drs. Eugene F. DuBois, Robert J. Carlisle, Linnaeus La Fetra, Charles E. Nammack and Van Horne Norris for permission to use reports from their services: We are indebted to Dr. Douglas Symmers for the use of the records of the pathologic laboratory.

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